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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/171,625	07/02/99	KOSTER H	24743-2302US

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EXAMINER	
PONNALURI, P	
ART UNIT	**PAPER NUMBER**
1627	12

DATE MAILED: 02/26/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/171,625	Koster et al
Examiner	**Group Art Unit**
P. Ponnaluri	1627

☒ Responsive to communication(s) filed on *Dec 4, 2000*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-36* is/are pending in the application.

Of the above, claim(s) *2, 5-10, and 17-36* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 3, 4, and 11-16* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5, 7*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. This application is a 371 of PCT/US97/06509, which claims benefit of provisional application 60/015,699 filed on 4/17/96.

2. Claims 1-36 are currently pending in this application.

3. Applicant's election with traverse of group I, claims 1, 3-4, 11-16, and species election with traverse of nucleoside (as low molecular weight compound), phosphate group (reactive group), and tritylether (linkage group), in Paper No. 11, filed on 12/4/00 is acknowledged. The traversal is on the ground(s) that the special technical feature of group I is not taught by the prior art. This is not found persuasive. Applicants point out that Carell et al do not teach combinatorial synthesis based on immobilized molecules. Applicants arguments have been considered. However, it is well known in the art to synthesize combinatorial library of compounds using solid supports and blocking groups. Thus, the inventions lack unity.

Applicants argue that the group IV inventions which are drawn to the products would have been combined with group I inventions. This is not persuasive, because it has been shown the special technical feature of group I, is method of synthesis, not the core compound with structure M, and group I do not even recite the core structure of core compounds. Thus, restriction is proper between groups I, and IV.

Applicants argue that the group III inventions which are drawn to the products would have been combined with group II inventions. This is not persuasive, because group II do not recite the core structure of compounds and the oligomers of group II would read on different

compounds with any different types of monomers, and do not require the monomers of group III. Thus, restriction is proper between groups II, and III.

The requirement is still deemed proper and is therefore made FINAL.

4. In the previous office action, the species election in pages 4-5 (groups e, f, g and h) should be applicable only when group IV is elected. These have been inadvertently included with group III.

5. Claims 20-22 and 36 were inadvertently not included in the groups, during restriction. Claims 20-22 are joined with Group III, (claims 17-22); and claim 36 is joined with group IV (claims 23-36).

6. Claims 2, 5-10, 17-36 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 11.

7. Claims 1, 3-4 and 11-16 are currently being examined in this application.

8. This application has been filed with informal drawings, and if applicant intends to renumber the informal figures, applicant is encouraged to amend the specification so that the description of the renumbered figures corresponds to the renumbered figures.

9. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: the specification do not have antecedent basis for the types of solid supports claimed in claim 14.

10. The use of the trademark MILLENNIUM (page 29), WATERS NOVA PAK (page 29) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

11. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

14. Claims 1, 3-4, 11-16 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

According to the text of 35 U.S.C sec. 101, an invention must be "useful". Our reviewing courts have applied the labels, "specific utility" (or "practical utility") to refer to this aspect of the "useful invention" requirement of sec. 101. (Nelson v. Bowler, 626 F.2d 853, 206 USPQ 881,

883 (CCPA 1980)). In Nelson, the court characterized "specific utility" (or "practical utility") as "a shorthand way of attributing real-world value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." (Id. at 856.)

The claimed method of generating a combinatorial set of compounds, are not supported by a specific asserted utility and do not, without further research and experimentation, provide an immediate benefit to the public. The final compounds (oligomers) generated using the claimed method are not supported by a specific asserted utility because the disclosed use(s) of the oligonucleotides is not specific and is generally applicable to any nucleic acid. The specification discloses that the compounds (oligonucleotides) are useful as drugs, which is not specific. The specification does not identify the compounds which would be useful as drugs. The specification failed to identify a specific utility for the claimed invention. Any benefit to the public (to one of ordinary skill in the art) is speculative. There is no basis in the specification upon which to conclude that *any* of the compounds encompassed by the library are, or will turn out to be, biologically active after testing. On pages 4-5 of the specification, applicant implies that the advantages of the claimed method to obtain nucleic acids with modified oligonucleotide back bone is not only speculative. The nucleic acid library prepared by the claimed method would require further research to identify useful oligonucleotides. Thus, the biomedical research is to take place at some future time, only when the properties of the claimed compounds have been elucidated by the experimental methods (screening assays). Absent a disclosure of those

properties, the asserted utility lacks specificity. Note, because the claimed invention is not supported by a specific asserted utility for the reasons just set forth, credibility cannot be assessed.

This is not to say that inventions that are to be used exclusively in a research setting (i.e., research tools) always lack a specific asserted utility. Indeed, many research tools such as telescopes, gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility. (See USPTO Utility Guidelines, page 12.) However, inventions that have a specifically identified utility must be distinguished from those whose utility requires further research to identify or reasonably confirm. Labels such as 'research tool' , 'intermediate', 'for research purposes' are not helpful in determining if an applicant has identified a specific utility for the invention. Research tools (such as gas chromatographs, screening assays, etc.) are useful in the sense that they can be used in conjunction with other method steps to evaluate materials other than themselves or to arrive at some result. The combinatorial libraries obtained by the claimed method are not research tools in this sense. Rather, they are themselves the subject of basic research, whose usefulness or lack thereof has yet to be established. Merely labeling the instant libraries as "research tools" does not impart the specific utility required by this statute.

In the absence of an asserted specific utility, the "useful" requirement may be established by reference to a well established utility. A "well established utility" is a "specific utility" which is well known, immediately apparent and implied by the specification based on the disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. The

combinatorial libraries obtained by the claimed process are not supported by a well established utility, however, because neither the specification as filed nor any art of record discloses or suggests any property or activity for the compounds such that another non-asserted utility would be well established for the compounds. Further, the compounds of the claimed libraries are not recognizable as analogous to compounds with a recognized pharmacological (or other) activity. In the absence of any data as to their activity, there is no basis upon which to base either a specific or a well-established utility.[1]

Claims 1, 3-4, 11-16 are also rejected under 35 U.S.C. § 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention.

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[1] Note that a "well established utility" cannot alternatively be based upon a "throw away" utility that one can dream up for an invention, or upon a utility that would obviously apply to virtually every member of a very general class of materials. If this were the case, any product or apparatus, including perpetual motion machines, would have a "well established utility" as landfill, an amusement device, a toy, or a paper weight, any carbon containing molecule would have a "well established utility" as a fuel since it can be burned, and any protein would have well established utilities such as manufacturing supplements for vitamins or food, as protein supplements for animal food, or as an animal poison in the protein is toxic. This is clearly not the intention of the statute. However, it is noted that if such utilities are specifically asserted by applicant in the specification, the would meet the utility requirement of 35 U.S.C sec. 101. See Utility Guidelines, pages 44-45.

15. Claims 1, 3-4, and 11-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims recite a process for generating a combinatorial set of molecules of core structure M.

The claims do not recite the core structure of the compounds or other identifying characteristics presented with respect to the final combinatorial compounds or for that matter the chemical reactants.

The specification description directed is directed to specific oligonucleotide combinatorial libraries which clearly do not provide an adequate representation regarding the open ended claimed library compounds made by the presently claimed invention.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Although directed to DNA compounds, this holding would be deemed to be applicable to any compound; which requires a representative sample of compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the claimed generic(s).

In the present instance, the claimed invention contains no identifying characteristics regarding the synthesize combinatorial library(ies).

Additionally, the narrow scope of examples directed to specific oligonucleotide compounds are clearly not representative of the scope of combinatorial library compounds of the presently claimed invention.

16. Claims 1, 3-4 and 11-16 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

17. Claims 1, 3-4, and 11-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of synthesis of oligonucleotides, does not reasonably provide enablement for synthesis of any other kind of compounds such as oligosaccharides, lipids, vitamins, hormones, peptides, or any other drug compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claims recite a process for generating a combinatorial set of molecules of core structure M with plurality of reactive moieties. The specification discloses oligonucleotide

combinatorial libraries and methods of making ht libraries. The specification disclosure does not have guidance to prepare any other kinds of combinatorial libraries. The factors in determining the undue experimentation are disclosed in *In re Wands* (U.S.P.Q. 2d 1400 (CAFC (1988)). The factors to be considered include; the quantity of experimentation necessary, the amount of guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the predictability of the art and the breadth of claims.

The specification discloses that using new protected schemes and solid phase synthesis, oligonucleotides are obtained. The specification does not give a guidance or direction in selecting a core molecule which has multiple reactive sites. The specification does not have guidance for preparation of any other molecules other than the oligonucleotides by derivitizing the reactive groups of the core structure M. The working examples disclosed in the specification are directed to methods of preparing oligonucleotides. The working examples do not include any preparation of carbohydrates, or peptides, or lipids or hormones by derivitizing the reactive moieties of the core structure. The state of the prior art is such that it is not clear which core structure is useful in preparing the libraries of compounds (carbohydrates, or peptides, or lipids or hormones). Thus, in the absence of adequate guidance in the specification, one skilled in the art would require undue amount of experimentation to prepare combinatorial set of compounds other than the oligonucleotides by derivitizing the core structure.

18. Claim 16 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 16 recites that the linkage is selected from the group consisting of tritylether, ...and derivatives thereof.

The specification disclosure clearly does not clearly an adequate representation regarding the open ended 'derivatives thereof' of the presently claimed invention.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Although directed to DNA compounds, this holding would be deemed to be applicable to any compound; which requires a representative sample of compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the claimed generic(s).

In the present instance, the claimed invention contains no identifying characteristics regarding the derivatives of the linkages.

19. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

20. Claims 1, 3-4 and 11-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites 'a combinatorial set of molecules of core structure M', it is not clear what does applicants mean by combinatorial set of molecules', applicants are requested to clarify.

Claim 1 recites 'preparing a plurality of immobilized compounds of core structure M', the claim does not define how the compounds are prepared which are immobilized. Applicants are requested to clarify.

Claim 1 recite 'said molecules contain a plurality of reactive moieties', clarification is requested what does applicant mean by molecules contain a plurality of reactive moieties. Does applicants mean that each molecule has more than one reactive moiety or reactive moieties on different molecules together is considered as plurality of reactive moieties.

Claim 1 recites that the 'at least three of the blocking groups are independently removable under at least three different conditions...', clarification is requested what does applicant mean by at least three blocking groups. Are these three blocking groups belong to the same compound or may belong to more than one compound of the immobilized molecules of the core structure M? If they belong to different compounds, it is not clear which compounds. It is not clear what does

applicants mean by independently removable under at least three different conditions. Clarification is requested what does applicants mean by at least three different conditions. What are the three different conditions. Applicants are requested to clarify.

Claim 1 recites 'removing certain blocking groups', clarification is requested what does applicant mean by certain blocking groups. Are these certain blocking groups are present on one compound or can be from different compounds? If the blocking groups are present on different compounds, it is not clear which blocking groups are removed. Is there any criteria in selecting the blocking groups which are removed. Applicants are requested to clarify.

Claim 1 recites 'preprogrammed, regioselective manner', clarification is requested what does applicants mean by preprogrammed. Does applicants mean that the blocking groups are removed using some automatic or robotic machine? It is not clear what does 'regioselective manner' is. Clarification is requested.

Claim 3 recites the limitation "the immobilized molecule" in line 1. There is insufficient antecedent basis for this limitation in the claim. Applicants are requested to amend the claim.

Claim 4 recites 'small molecule drug compound', clarification is requested what does applicant mean by small molecule drug. The specification disclosure does not have any specific definition or description of small molecule drug compounds, and it is not clear which compounds are considered as small molecule drug compounds.

Claims 11 and 12 are dependent on non elected claim 2, applicants are requested to 'cancel claim 2' in the claims.

Claim 12 recites the limitation "the molecule" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 13 recites the limitation "the bottom of a microtiter" in line 3. There is insufficient antecedent basis for this limitation in the claim.

Claim 13 recites improper Markush group 'selected from the group consisting of beads, wafers with or without pits and/or channels, the bottom of microtiter plate or inner walls of a capillary.' Applicants are requested to amend the claim as "selected from the group consisting of beads, wafers with pits, wafers without pits, wafers with channels, wafers without channels, bottom surface of a microtiter plate and inner walls of capillary tubes."

Claim 14 contains the trademark/trade name SEPHADEX, SEPHAROSE, TEFLON. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe solid supports and, accordingly, the identification/description is indefinite.

Claim 15 recites 'can be' which makes the claim indefinite. Applicants are requested to amend the claim.

Claim 16 recites 'derivatives thereof', clarification is requested what does applicants mean by derivatives thereof. The specification disclosure does not have support for derivatives of all the groups. Applicants are requested to clarify.

21. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

22. Claims 1, 3-[illegible] and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Montal et al (Proceedings of the National Academy of Sciences of the USA, vol. 87, No. 18, pages 6929-6933, 1990).

The instant claims briefly recite a method for generating a combinatorial set of molecules of core structure M, comprising: a) immobilizing a plurality of compounds of core structure M, the compounds have plurality of reactive groups, and the reactive groups are blocked by blocking groups; and b) removing certain blocking groups and derivatizing the unblocked reactive groups with substituent and thereby forming a combinatorial set of molecules.

Montal et al discloses a synthetic proteins. The reference discloses that a tethered parallel tetramer was synthesized by attaching to a carrier template - a 9-amino acid backbone (K*KK*PGK*EK*G) (see figure 1 A) with four attachment sites (K*) (refers to the core

structure with plurality of reactive sites of the instant claims) (see the abstract). The reference discloses that the template was synthesized using solid phase techniques (refers to molecule immobilized of the instant claims). The reference discloses that oligopeptides (refers substituents of the instant claims) are attached to the template in a stepwise manner at the 4-base-deprotected lysine side chain (refers to step b of the instant claims) (see page 6931, under experimental results) . The reference discloses that the completed 101 residue proteins (refers to a combinatorial set of molecules of the instant claims) are cleaved from the support (see page 6931). The template a 9-amino acid backbone (K*KK*PGK*EK*G) of the reference clearly reads on the multi functional low molecular weight compound of the general formula MD_n (instant claim 3) and amino acid of instant claim 4; and the reactive moieties of the amino acid template of the reference would read on the reactive moieties of the instant claim 11. Thus the reference clearly anticipates the claimed invention.

23. Claims 1, 3-4, 11-16 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 95/13538 (SAUL et al).

Saul et al disclose methods for producing and screening complex chemical libraries (see abstract). The reference discloses a polyfunctional core molecule (refers to core structure M of the instant claims) may have different functionalities having similar activity to the reactants. The reactants react with the functionalities of the core molecule (refers to core structure with plurality of functionalities of the instant claims) (see page 5). The different functionalities on the core molecules react with the reactants to form all possible combinations of the products (see page 5).

The reference discloses that the core molecule may be free in solution or be bound to a solid support (refers to immobilized molecules of core structure M of the instant claims), whereas the solid support may be resins, solid surfaces such as magnetic particles, porous glass beads, polyethylene pins (refers to instant claims 13-14) (see page 16, 2nd paragraph). The reference discloses that the core molecule is joined to particle by a functionality which is cleavable (refers to instant claim 12) , the thiophenyl ethers (refers to tritylether of claim 16) may be cleaved by mercuric trifluoroacetate fluoride, nitrobenzyl ethers which can be cleaved by photolysis (refers to instant claim 15) (see pages 16-17). The reference discloses that the core molecule may be aliphatic, alicyclic, aromatic or heterocyclic, wherein the heteroatoms usually be nitrogen, oxygen, sulfur, phosphorus, metal atoms, boron etc (see page 18), and core molecules will have usually have at least three reactive functionalities, and not more than 10 active functionalities (see page 18). The reference discloses that the compounds of interest as core molecules include sugars, such as mono, and disaccharides, polyfunctionalized aromatic compounds (refers to instant claims 3 and 4) (see page 19). The reference discloses that protective groups may have been employed with the reactive functionalities (refers to blocking groups of the instant claims). The reference clearly anticipates the claimed invention.

24. Claims 1, 3-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Stengele et al (Tetrahedron Letters, Vol. 31, No. 18, pp2549-2552, 1990) (reference BG, in the PTO 1449, filed by applicants on 11/3/99).

Stengele et al disclose improved synthesis of oligodeoxyribonucleotides. The reference discloses that the synthesis of 3'-(2-cyanoethyl)-N, N-diisopropylamido-phosphites differs from the commonly used building blocks (refers to core molecules of the instant claims) by applying p-nitrophenylethoxycarbonyl (NPEOC) group for amino protection instead of the benzoyl and isobutyl group and the additional blocking amide function of 2'-deoxyguanosine by the p-nitrophenylethyl (NPE) residues (see page 2549 and the reaction scheme in page 2551). In the reaction scheme, oligonucleotide (refers to core molecule of the instant claims) with multiple blocking groups, NPE, NPEOC (refers to step a, of the instant claims, and the reaction refers to step b of the instant claims). The reference discloses that the advantage of NPE/NPEOC-strategy. The reference discloses that first 5'-O-dimethoxytrityl group is removed, and then NPE and NPEOC are removed, to obtain totally deprotected oligonucleotide still attached to the solid supports. The reference discloses that the instant method is superior to known methods. The reference discloses that the dihydroxypropyl-CPG beads (refer to instant claims 13, 14 of the instant claims). The reference discloses that the beads are reacted with an aliphatic secondary amine spacer (refers to instant claim 12), and the cleavage of the compound (oligonucleotides) from the support using concentrated ammonia (refers to instant claim 15). The reference discloses that several oligonucleotides are synthesized using DNA synthesizer. The reference clearly anticipates the claimed invention.

25. No claims are allowed.

Any inquiry concerning this communication should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat, can be reached at (703)308-2439. The fax number for this group is (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703)308-0196.

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22 February 2001